

Letter to the Editor

Pseudoresistance to permethrin in scabies

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Abstract

Reports of permethrin resistance of *Sarcoptes scabiei* var. *hominis* are emerging. We propose that this may be pseudoresistance. The resistance is due to inadequate counselling by physicians, incorrect treatment (insufficient quantity of permethrin; too short length of treatment), and poor adherence and compliance by patients. Other reasons include single application of permethrin, suggestion to apply the drug for 6-8 hours, failed application on subungual folds, irritant contact dermatitis, in particular on genitals, for which some patients stop the treatment, and unexplainable use of permethrin in post-scabies prurigo. Thus, we believe that several cases of resistance to permethrin are actually cases of pseudoresistance.

Key words: *Sarcoptes scabiei* var. *hominis*; scabies; permethrin; pseudoresistance; resistance.

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Dear Editor,

In recent times, some articles have reported the emergence of *Sarcoptes scabiei* var. *hominis* resistance to permethrin [1]. We present our experience acquired in recent years in African patients with scabies. These patients were migrants who came from Egypt, Senegal, Niger, Mali, Ethiopia and Eritrea, and were observed in Milan, Italy, by two authors (SV and RS). It is necessary to distinguish pseudoresistance from true resistance. We hypothesize that pseudoresistance is much more frequent than resistance.

Causes of pseudoresistance

Incorrect Treatment

In our experience, some common causes of pseudoresistance are inadequate counselling by physicians, incorrect treatment (insufficient quantity of permethrin; too short length of treatment) and poor adherence and compliance by patients. Furthermore, companies that sell permethrin are responsible for incorrect information. Some companies put out statements such as “in 90% of cases, a single application of 5% permethrin is sufficient to eliminate the infestation”. We know that this is very rarely true; permethrin must be reapplied 7 to 10 days after the first application. This is because eggs hatch after 2 to 10 days (usually after 6 to 7 days). Another questionable

statement is that “permethrin must be left on the skin for at least 8 hours”. Again, this is not true: it must be left on the skin for 12 hours [2]. This apparently long permanence of permethrin on the skin does not increase the toxicity of the drug. In humans, lethal oral dose of permethrin is 1-2 g/kg. After topical application, permethrin is rapidly metabolized in the skin. It is absorbed in small amounts and is almost completely excreted through urine. Elimination is complete after one week and no risks of tissue storage exist [3-7]. Therefore, the application of permethrin for 12 hours does not induce a systemic absorption. This is important because, as previously mentioned, many leaflets of permethrin products marketed in Europe suggest that the cream should be applied for not more than 6-8 hours.

An additional, important cause of pseudoresistance is the location of the mite. We know that common locations of scabies are axillae, elbows, wrists, interdigital folds of the hands, breasts, penis, scrotum and buttocks. Published data on nail involvement are insufficient and limited to anecdotal cases. However, subungual skin of fingers is much more frequently involved than previously thought [8]. Eighty-nine Caucasian immunocompetent patients (51 males and 38 females, aged 18-74 years), with a clinical diagnosis of scabies, were subjected to microscopical examination

in order to confirm the diagnosis. In all patients, fourteen locations (chest, breasts, axillae, elbows, wrists, interdigital folds of the hands, subungual skin of fingers, abdomen, pubis, penis, scrotum, vulva, back and buttocks) were evaluated. Microscopical examination was considered positive when mites and/or eggs and/or faeces were observed. In males, the more frequently involved area was penis (34/51 = 66.7%), followed by scrotum (26/51 = 51%) and subungual skin of fingers (21/51 = 41.2%). In females, microscopical examination was positive in breasts (23/38 = 60.5%), followed by axillae (15/38 = 39.5%) and subungual skin of fingers (14/38 = 36.8%) [8]. Neither burrows nor other lesions in subungual skin of fingers were observed in all patients. In 5/21 males (23.8%) and 2/15 females (13.3%) only mild subungual scales were observed. In addition, no patient complained of itching in peri- and subungual skin of fingernails [8]. Nail involvement is well known in crusted scabies: it is characterized by yellow pigmentation of the nail plate and nail bed hyperkeratosis. However, as previously mentioned, nail involvement was very rarely reported in classical scabies. In conclusion, subungual skin of fingernails is a frequent location of scabies, although no typical lesions, except for rare thin scales in some patients, were observed in these areas, and no itching was reported by patients [8]. It is possible that scabies mites find a favourable environment beneath the free edge of nail plates. These observations suggest that treatment should include peri- and subungual skin of fingers in all patients with scabies. The fingernails should be trimmed very short, scrubbed with a brush and treated with specific therapy. This procedure can reduce the incidence of both resistance and pseudoresistance [8].

Side Effects

One more reason of pseudoresistance of scabies to permethrin is irritant contact dermatitis. We know that allergic contact dermatitis caused by permethrin is extremely rare. However, permethrin can induce an irritant contact dermatitis. In our experience, more than 5% of patients stop the treatment because of this dermatitis. The most frequent reason is an important burning sensation on genitals, specifically in the glans. It is possible to reduce incidence and severity of this dermatitis by storing the cream in the refrigerator and applying as cool cream. The storage of permethrin in refrigerator does not influence its clinical efficacy: it has been demonstrated that both cis and trans isomers of permethrin are highly stable at different temperatures [7].

Another Diagnosis

Finally, it is necessary to discuss the differential diagnosis of post-scabies prurigo with nodular scabies [8]. Post-scabies prurigo is a common complication of scabies. It is caused by a delayed, chronic hypersensitivity reaction to antigens of the mite, such as proteolytic enzymes produced by females for the construction of the burrows, metabolic products released by the mites during the moults or after their death, saliva and faeces. Diagnosis of post-scabies prurigo is based on history of successfully treated scabies; presence of reddish-brown, round, papular-nodular lesions, severe pruritus, negative microscopical/dermatoscopical examinations for mites, eggs and faeces, ineffective anti-scabies therapy, and recovery by means of potent topical corticosteroids [9]. This distinction is important because we weekly observe that post-scabies prurigo is chronically, although unsuccessfully, treated as nodular scabies. A microscopical and/or dermatoscopical examination of the lesions is mandatory.

Conclusions

In summary, it is possible that scabies may have become less sensitive to permethrin than in the past. However, it is also possible that several cases of resistance are actually cases of pseudoresistance. In order to reduce pseudoresistance, it is necessary: a) to leave permethrin for 12 hours, b) to apply permethrin 7 to 10 days after the first application, c) to treat the nails carefully, d) to apply permethrin as cool cream and e) to distinguish nodular scabies from post-scabies prurigo.

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